

Application No. 09/938,763

RD-28250

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of

James N. CAWSE

Group Art Unit: 1631

Application No.: 09/938,763

Examiner: Cheyne D. Ly

Filed: August 27, 2001

For: METHOD AND SYSTEM TO INVESTIGATE A COMPLEX
CHEMICAL SPACE

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- (1) **REQUEST FOR RECONSIDERATION UNDER 37 C.F.R. §1.116**

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Application No. 09/938,763

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**RESPONSE UNDER 37 CFR §1.116
EXPEDITED PROCEDURE
EXAMINING GROUP 1631**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of

James N. CAWSE

Group Art Unit: 1631

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REQUEST FOR RECONSIDERATION UNDER 37 C.F.R. §1.116

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Sir:

Claims 1 to 7, 9 to 10, 13 to 36 and 39 to 42 are pending. The September 22, 2003 Final Rejection rejected claims 1, 10, 20, 35 and 36 under 35 U.S.C. 112, second paragraph; claim 16 under 35 U.S.C. 112, first paragraph;¹ claims 1 to 7, 9, 10, 13 to 28, 34 to 36 and 39 to 42 under 35 U.S.C. 103(a) over Agrafiotis et al. and Grate et al. and claims 1 to 7, 9, 10, 13 to 36 and 39 to 42 under 35 U.S.C. 103(a) over Agrafiotis et al., Grate et al. and Chaudhari et al. Reconsideration is requested for the following reasons:

¹ The Final Rejection also states that "[t]he rejection is maintained with respect to claims [sic, claim?] 6, as recited in the previous office action Paper No. 8, mailed May 15, 2003. It is believed that this statement is intended to refer to claim 16, not claim 6, since claim 6 was not rejected under 35 U.S.C. 112, second paragraph in the previous office action. If Applicant is incorrect, the PTO is respectfully requested to withdraw the final rejection and to reissue another non-final rejection that clarifies and explains a claim 6 rejection and restarts the period for response.

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I. REJECTION OF CLAIMS 1, 10, 20, 35 AND 36 UNDER 35 U.S.C. 112, SECOND PARAGRAPH

Claims 1, 10, 20, 35 and 36 were rejected under 35 U.S.C. 112, second paragraph.

A. Claim 1

The Final Rejection, pages 2 to 3 states:

Specific to claim 1, lines 14 and 15, the term "outside" causes the claim to be vague and indefinite because it is unclear as to what criteria are being used to determine that specific identified effects are outside the standard deviation (greater or less than). Clarification of the metes and bounds is required.

However, the term used is not "outside"; the term is "outside a standard deviation," a term well supported in the specification paragraphs [0026] and [0027] and a term that clearly establishes the "outside" criteria.

The Office Action page 9 states:

However, Applicants do not set forth the criteria that are used to determine that specific identified effects are outside the standard deviation (greater or less than).

However, the term "outside a standard deviation" is well known to those skilled in the art. For example, see McClendon et al., Pat. 5,856,929. A "standard deviation" is the "metes and bounds." A standard deviation is "a measure of the dispersion of a frequency distribution that is the square root of the arithmetic mean of the squares of the deviation of each of the class frequencies from the arithmetic mean of the frequency distribution," Merriam Webster's Collegiate Dictionary, 10th Ed., p. 1146 (1993). As shown in the specification and as is well-known in the art, if a specific identified effect is outside a deviation as defined by a standard it is "outside the standard deviation." This basis for the rejection should be withdrawn.

B. Claim 10

The September 22 Office Action states:

Specific to claim 10, (ii), the variables X' and X are vague and indefinite.

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The said variables in step (i), claim 10, represent two different matrices. However, in another interpretation, the said variables represent numerical values to which the post-multiplying step is performed. Is the post multiplying step performed using the matrices X and X' or the numerical values representing by the variables X and X' ?

This is the precise argument – word for word - that the PTO presented in

In response, Applicant argued:

The PTO argument is incorrect. The X' , X and y notations are well known and conventional matrix algebra notations. See for example, <http://www.itl.nist.gov/div898/handbook/pmc/section5/pmc53.htm>. The X' , X and y notations are defined and exemplified in the specification. For example, see the specification paragraphs [0020] to [0024]. The X' , X and y notations are defined in the claims themselves. See claim 1 for example. The meanings of the notations are consistent throughout the specification and claims. One skilled in the art is apprised of the scope of the claims in this respect. See *Seattle Box Co., v. Industrial Crating & Packing, Inc.*, *supra*. This basis of the 35 U.S.C. § 112, second paragraph rejection should be withdrawn.

July 23 2003 Amendment, page 11.

The September 22, 2003 Final Rejection argues:

Applicants argue that notations X' , X , and y are well known in the art via pointed to support from a website and the instant specification has been fully considered and found to be unpersuasive. Applicants disclose "matrix operations can include representation (posing or modeling data in a matrix representation), addition... and distribution (assigning a probability value)" [0019]. The disclosure set forth above further support the unclarity [sic] of the claimed invention because it is unclear whether the post-multiplying step [sic, is?] performed using the matrix representation or the numerical values representing by the variable.

September 22 Final Rejection, pages 3 to 4.

First, it is impossible to understand the PTO's position from its response. Is the PTO arguing that matrix algebra is not well known or that the claim nomenclature is not conventional matrix algebra notations?

Second, whether claims are definite under 35 U.S.C. § 112, second paragraph, is determined in light of the specification. The specification does not "further support...

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unclearly [sic]." The specification can clarify meaning of the claims. The *claims read in light of the specification* need only apprise those skilled in the art of the scope of the invention. *Hybritech v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1387, 231 USPQ 81, 94, 95 (Fed. Cir. 1986), cert. denied 480 US 947 (1987) (emphasis added).

Third, the PTO "short cuts" Applicant's argument. Applicant's argument is that the notations are well known and are conventional matrix algebra notations. A copy of <http://www.itl.nist.gov/div898/handbook/pmc/section5/pmc53.htm> is attached. Applicant's specification states:

[0019] The results from the CHTS experiment are analyzed using matrix algebra to extract combinations of the experiment interactions. A mathematical matrix is a representation of real numbers in a rectangular array. Matrices are important tools for expressing and discussing problems that may involve complex data sets. Matrix analysis is a multivariate methodology for expressing and manipulating these kinds of data and for solving problems posed by the data. Matrix operations can include representation (posing or modeling data in a matrix representation), addition, subtraction, scalar multiplication, matrix multiplication, multiplication by inverse, transposition (interchanging rows and columns) and distribution (assigning a probability value). Matrices can be manipulated to produce a sum, difference, scalar multiple, matrix multiple, product or transpose.

[0020] In the present invention, the matrices are representations of CHTS results in a rectangular array. The runs from the CHTS experiment provide sets of results or y 's, one for each run, each correlated with a set of levels of factors, x_i . Each run y is associated with an error e . Each of the factors or interactions is associated with a coefficient β . These elements (x 's, their interactions and y 's) can be represented in vector/matrix form as shown in FIG. 3, wherein levels of factors and interactions form a rectangular array or matrix (20) of scalar values X . Further in FIG. 3, y 's, β 's and e 's are represented in single column matrices (10), (30), and (40). A matrix estimation equation of the system can be as follows:

$$y = X \beta + e \quad (I)$$

[0021] where X is a matrix of factor and interaction levels in the experiment, y is a matrix of experimental results, β is effects (both main effects and interaction effects), every e_i in e has the same variance σ^2 , error terms e_i arise from a normal distribution and expected value $E(y)$

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(definition: the value of the response if no error is present) of the response is $E(y) = X\beta$

[0022] The method involves solving the above matrix estimation equation (I), according to the relationship:

$$\beta = (X'X)^{-1}X'y \quad (II)$$

[0023] where superscript ' indicates a transpose of a matrix (in which each row becomes a column and each column a row). The superscript $^{-1}$ indicates an inverse function of a matrix. Thus for any square matrix A, a relation can be defined as $AA^{-1} = I$, where I is the identity matrix 50 shown in the FIG. 3 model.

[0024] Accordingly, results can be assembled as an $n \times 1$ vector y and factor level values can be assembled into an $n \times k+1$ matrix X with 1's as designations in a first column and each other column containing the coded factor level values (+1's and -1's representing the extents of the values of the factors and interactions). Matrix equation (I) is then solved for effects parameters β .

[0025] The effects parameters of matrix β are then examined for statistical significance. The null hypothesis can be applied in this examination. The null hypothesis is that all of the effects observed in the experiment are caused simply by random processes. If this is correct, the effects will fit to a normal distribution and form a relatively straight line in a probability plot. In FIG. 4; E100 is a straight line representing a results approximation. The line is flanked by dashed lines denoting multiples of standard deviations. A desired standard deviation can be selected by an experimenter for the experiment. Any effects that fall off the line by more than the standard deviation can be interpreted to have been caused by nonrandom processes, as taught by D. Montgomery, Design and Analysis of Experiments, 3rd Ed., John Wiley, 1991, NY, p 99. Effects that positively exceed the deviation can represent combinations that are failures or combinations that provide synergistic improvement, i.e., leads.

[0026] In a preferred embodiment, results from the CHTS method are analyzed by matrix algebra by steps of (A) representing the results as an $n \times 1$ matrix y where n = a number of factor level combinations in the experiment, (B) representing extents of the factor level combinations in an $n \times n$ matrix X, (C) solving n simultaneous equations represented by the matrices according to matrix algebra to form a results matrix β and (D) examining the results matrix β to identify effects outside a standard deviation.

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[0027] The step (B) can comprise coding extents of the factor level combinations as a +1 or -1 and representing the coded extents as the $n \times 1$ matrix y . The step (C) can comprise (i) transposing matrix X to form matrix X' , (ii) postmultiplying X' by X to generate a matrix and (iii) postmultiplying the generated matrix by y to form the results matrix β . The step (D) can comprise (i) representing the results matrix β as a normal probability plot, defining a standard deviation for results of the plot and (iii) identifying positive interactions outside of the standard deviation. The standard deviation can represent a probability that a result deviation from the standard is random and that positive interactions can be identified outside of the deviation. In one embodiment, the probability can be established at 95 percent or better to define an experimental space for a commercial process or the probability can be established at 99.7 percent or better to define a best set of factor levels as leads for a commercial process.

The teachings of Applicant's specification and <http://www.itl.nist.gov/div898/handbook/pmc/section5/pmc53.htm> are not exhaustive of the knowledge in the art. The teachings of Applicant's specification and <http://www.itl.nist.gov/div898/handbook/pmc/section5/pmc53.htm> are only examples of how well known matrix algebra notation is. For other examples, the PTO's attention is directed to Krishnan Namboodiri et al., "Matrix Algebra: An Introduction," SAGE Publications, 1 (1986) and to the literally hundreds of patents that refer to matrix algebra noted on the attached PTO data base print out.

Fourth, the "post-multiplying" is described in the specification paragraph [0027] and elsewhere. Paragraph [0027] states:

The step (B) can comprise coding extents of the factor level combinations as a +1 or -1 and representing the coded extents as the $n \times 1$ matrix y . The step (C) can comprise (i) transposing matrix X to form matrix X' , (ii) postmultiplying X' by X to generate a matrix and (iii) postmultiplying the generated matrix by y to form the results matrix β . The step (D) can comprise (i) representing the results matrix β as a normal probability plot, defining a standard deviation for results of the plot and (iii) identifying positive interactions outside of the standard deviation. The standard deviation can represent a probability that a result deviation from the standard is random and that positive interactions can be identified outside of the deviation. In one embodiment, the probability can be established at 95 percent or better to define an experimental space for a commercial process or the probability can be established at 99.7 percent or better to define a best set of factor levels as leads for a commercial process.

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Again, the claims must be read in view of the specification, *See Hybritech v. Monoclonal Antibodies, Inc., supra*. As is known in matrix algebra, and as indicated by these specification passages, if the matrix' represent specific values, then specific values are multiplied for a solution. On the other hand, consistent with conventional algebraic expression, if the matrix' represents variables, then the multiplying solution is a variable.

Claim 10 distinctly claims the invention and this basis for therejection under 35 U.S.C. 112, second paragraph rejection should be withdrawn.

C. Claims 20, 35 and 36

The Final Rejection rejects claims 20, 35 and 36 under 35 U.S.C. §112, second paragraph but fails to address these claims in the body of the rejection. No explanation is given for the rejection. The PTO is respectfully requested to withdraw the present office action and to issue a new office action to explain the rejection, restarting the period for response or withdraw the rejection of claims 20, 35 and 36.

For this and the above reasons, the rejection of claims 1, 10, 20, 35 and 36 under 35 U.S.C. §112, second paragraph should be withdrawn.

II. REJECTION OF CLAIM 16 UNDER 35 U.S.C. 112, FIRST PARAGRAPH

Claim 16 was rejected under 35 U.S.C. 112, first paragraph.

The May 15, 2003 Office Action applied the same rejection to claim 16. Applicant responded that the specification provides an enabling disclosure of claim 16. The September 22, 2003 Final Rejection states:

Applicants argue the specification enable [sic, enables?] the invention of claim 16 due to said claim does not claim a commercial process.

This is a "short-cut" mischaracterization of Applicant's argument. Applicant's argument is that "[c]laim 16 does not claim a commercial process; claim 16 claims a process that identifies a "best set of factor levels [that define] *leads for a commercial process*"(claim 16, emphasis added). The specification teaches this process throughout the specification, from page 3, paragraph [0010] to the specification end, including the

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drawings.”

The September 22, 2003 Final Rejection then states

Applicants' argument have been fully considered and found to be unpersuasive because the scope of the instant claim 16 includes the critical limitation of a commercial process. It is re-iterated the instant "invention provides a particularly well-suited experimental methodology to investigate multiple and complex interactions of a catalyzed chemical reaction" (page 3, lines 13-20). However, the instant application does not provide guidance or working examples for translating an experimental methodology for generating leads to a generic commercial process for using the said leads. It is well established that experimental methods require many iterations of trial and errors processes to refine an experimental process to a commercial process. Therefore, The instant specification does not provide sufficient guidance or working examples for one skilled in the art to predictably use the claimed invention for a commercial process.

First, a limitation "wherein the best set of factor levels defines leads for a commercial process" (claim 16) does not expand a claim to claim a "commercial process." The limitation only further *limits* the factor levels iterated in a preceding claim.

Second, a statement in the specification that an "invention provides a particularly well-suited experimental methodology to investigate multiple and complex interactions of a catalyzed chemical reaction" does not expand a claim limitation "wherein the best set of factor levels defines leads for a commercial process" (claim 16) to claim a "commercial process." The statement only further enables the broader invention by teaching a further utility.

Claim 16 does not claim a commercial process. Claim 16 claims "[t]he method of claim 15, wherein the best set of factor levels defines leads for a commercial process." Claim 16 claims "[a] method, comprising: defining an experimental space of a catalyzed chemical reaction to represent at least three factor interactions...." (independent claim 1). The specification provides an enabling disclosure of the claim 16 method "comprising defining an experimental space of a catalyzed chemical reaction." The rejection of claim 16 under 35 U.S.C. 112, first paragraph should be withdrawn.

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III. 35 U.S.C. 103(a) REJECTIONS

Claims 1 to 7, 9, 10, 13 to 28, 34 to 36 and 39 to 42 were rejected under 35 U.S.C. 103(a) over Agrafiotis et al. and Grate et al. and claims 1 to 7, 9, 10, 13 to 36 and 39 to 42 were rejected under 35 U.S.C. 103(a) over Agrafiotis et al., Grate et al. and Chaudhari et al.

These rejections are based on improper combinations of references without the motivation to combine required by *In re Lee*, 277 F.3d 1338, 61 USPQ 2d 1430 (Fed. Cir. 2002). Additionally, even if improperly combined, the references do not make out a *prima facie* case of obviousness. See *In re Deuel*, 34 USPQ2d 1210 (Fed. Cir. 1995).

A. IMPROPER COMBINATION OF REFERENCES

The Agrafiotis et al., Grate et al. and Chaudhari et al. references are not properly combinable.

The Agrafiotis et al reference relates to a synthesis protocol with re-iterated synthesis steps based on "structure-activity models" (Abstract). Grate et al. discloses "analyzing [a] sample with a multivariate instrument," for example, acoustic wave sensors (col. 9, lines 56 to 65). Chaudhari et al. is a commonly assigned patent that teaches reacting a hydroxyaromatic compound with oxygen and carbon monoxide in the presence of a VIIIIB catalyst to synthesize a diaryl carbonate (Abstract). The invention is a method of defining an experimental space for a CHTS method (claim 1).

The PTO has not provided the "reason to combine" showing required by *In re Lee*, 277 F.3d 1338, 1343, 61 USPQ 2d 1430, 1433-1434 (Fed. Cir. 2002) to support a combination of references rejection. A reference that teaches only "analyzing [a] sample with a multivariate instrument" (Grate et al.) and a diaryl carbonate synthesis method are not "reasonably pertinent" to a method of defining an experimental space for a CHTS method. The references are not properly combinable with the Agrafiotis et al reference as analogous art. See *In re Clay*, 23 USPQ2d 1058, 1060 (Fed. Cir. 1992).

To support a rejection based on a combination of references, "[t]he PTO "must

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not only assure that... requisite findings are made, based on evidence of record, but must also *explain the reasoning by which the findings are deemed to support the agency's conclusion*" (emphasis added). *In re Lee*, *supra* 61 USPQ 2d at 1434, 277 F.3d at 1343 (Fed. Cir. 2002).

To support a rejection based on a combination of references, "[t]he PTO "must not only assure that... requisite findings are made, based on evidence of record, but must also *explain the reasoning by which the findings are deemed to support the agency's conclusion*" (emphasis added). *In re Lee*, *supra* 61 USPQ 2d at 1434, 277 F.3d at 1343 (Fed. Cir. 2002). To establish a prima facie case of obviousness based on a combination of references, the PTO must provide an:

...objective teaching... [that] would lead [one skilled in the art] to combine the relevant teachings of the references." *In re Fritch*, 972 F.2d 1260, 1265, 23 USPQ2d 1780, 1783 (Fed. Cir. 1992)

... "When patentability turns on the question of obviousness, the search for and analysis of the prior art includes evidence relevant to the finding of whether there is a teaching, motivation, or suggestion to select and combine the references relied on as evidence of obviousness. See, e.g., McGinley v. Franklin Sports, Inc., 262 F.3d 1339, 1351-52, 60 USPQ2d 1001, 1008 (Fed. Cir. 2001) ("the central question is whether there is reason to combine [the] references," a question of fact drawing on the Graham factors)."

....

...The Board [PTO] must identify specifically the principle, known to one of ordinary skill that suggests the claimed combination. In other words, the Board must explain the reasons one of ordinary skill in the art would have been motivated to select the references and to combine them to render the claimed invention obvious."); *In re Fritch*, 972 F.2d 1260, 1265, 23 USPQ2d 1780, 1783 (Fed. Cir. 1992) (the examiner can satisfy the burden of showing obviousness of the combination "only by showing some objective teaching in the prior art or that knowledge generally available to one of ordinary skill in the art would lead that individual to combine the relevant teachings of the references").

In re Lee, *supra* 277 F.3d at 1343, 61 USPQ 2d at 1433-1434.

In response to this important requirement, the September 22 Final Rejection

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states:

It is noted that Agrafiotis et al. discloses an improvement for a general system and method for efficiently and effectively generating of chemical entities with defined physical, chemical or bioactive properties for drug lead identification via a chemical library (column 1, lines 15-23 and column 3, lines 27-29). The suggested improvement of Agrafiotis et al. is directly applicable to generation of chemical [sic, chemicals?] for the characterization, classifying, and identifying as taught by Grate et al.

Final Rejection, page 8.

This argument is incorrect for a number of reasons. First, Agrafiotis et al. and Grate et al. do not teach or suggest that any method for "generation of chemical entities" is applicable to a "classifying and identifying" method. Particularly, Agrafiotis et al. and Grate et al. do not teach or suggest that the Agrafiotis et al. method for "generation of chemical entities" is applicable to a "fundamentally different way to characterize chemical [sic, chemicals?] in a sample and to use that characterization to classify and possibly to identify the "chemical" as taught by Grate et al. (col. 11, lines 43 to 46). Indeed, the Grate et al. teaching of a "fundamentally different way" (emphasis added), is a teaching away from applicability (combinability) of the Agrafiotis et al. "classifying and identifying" method. See *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984). If the PTO disagrees, the PTO is respectfully requested to point out the applicability (combinability) teaching in the references.²

The September 22 Final Rejection argument continues:

An artisan of ordinary skill in the art at the time of the instant invention would have been motivated to partake the concept emphasized by Agrafiotis et al. for an iterative process for generating chemical entities with defined physical properties and/or bioactive properties (Abstract etc.) and improve on it by utilizing the method of Grate et al. which comprises using the properties chemical entities to identify a

² "[W]hen the PTO asserts that there is an explicit or implicit teaching or suggestion in the prior art, it must indicate where such a teaching or suggestion appears in the reference...." In re Rijckaert, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993).

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chemical sample.

Final Rejection, page 8.

However, again the Final Rejection fails to point out where any such motivation appears in the references. Applicant has examined both the Agrafiotis et al. and Grate et al. references. Contrary to the PTO argument, Agrafiotis et al. and Grate et al. do not teach or suggest any motivation or need to improve the Agrafiotis et al. method for "generation of chemical entities" by a "classifying and identifying" method (Grate et al.). Again, if the PTO disagrees, the PTO is respectfully requested to point out the applicability (combinability) teaching in the references. See footnote 2.

The September 22 Final Rejection concludes:

Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention was made to use the method of Agrafiotis et al. for generating chemical entities and determining the properties directed to the chemical entities; and identify and characterize the said chemical entities according to the method of Grate et al, which comprises an algebra matrix for identifying a sample.

Final Rejection, page 8.

But each premise purported to support this conclusion is incorrect. As pointed out above, Agrafiotis et al. and Grate et al. do not teach or suggest (1) that any method for "generation of chemical entities" is applicable to a "classifying and identifying" method, (2) that a method for "generation of chemical entities" is applicable to a "fundamentally different way to characterize chemical[s]" or (3) motivation or need to improve the Agrafiotis et al. method for "generation of chemical entities" by a "classifying and identifying" method (Grate et al.).

Similarly, the PTO has not provided any "logical and rational" reasoning to combine Chaudhari et al. The Final Rejection concludes that "[t]he suggested improvement of Agrafiotis et al. is directly applicable to generation of chemical for the characterization, classifying, and identifying as taught by Grate et al. and Chaudhari et al.," and that one would have been motivated to combine the Agrafiotis et al. "generation

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of chemical entities" with a "classifying and identifying" method teaching with "determining the properties as directed to the said chemical entities... including such chemical entities as catalysts (palladium and halide composition) and inorganic catalysts as taught by Chaudhari et al." However, the PTO provides no basis in the references for doing so and provides no "logical and rational" reasoning to support the PTO's conclusion that Chaudhari et al. is combinable with the other references.

The PTO has not provided any "logical and rational" reasoning to support its determination (to reject on combined references). *In re Lee*, *supra* 277 F.3d at 1342, 61 USPQ 2d at 1432-1433. The rejection is based on a selective picking and choosing of features in secondary references, without any basis in the references for doing so. The rejection is supportable only through hindsight. See *In re Deuel*, 34 USPQ2d 1210, 1215 (Fed. Cir. 1995). Unless the PTO can meet the required *In re Lee* "logical and rational" reasoning to combine, the rejection should be withdrawn.

B. NO PRIMA FACIE CASE

Further even improperly combined, the references do not establish a prima facie case of obviousness of any of (1) defining an experimental space of a catalyzed chemical reaction to represent at least three factor interactions (claims 1 to 7 and 18 to 33); (2) analyzing combinatorial results according to matrix algebra to select a best case set of factor levels from a catalyzed experimental space (claims 1 to 7 and 18 to 33); (3) conducting a CHTS on qualitative and quantitative factors (claim 35); (4) a programmed controller that analyzes CHTS results according to matrix algebra (claims 36 and 39 to); (5) defining a space to represent "at least 6 orders of interaction of factors" of a catalyzed chemical reaction (claim 5); (5) defining a space to represent "at least 6 orders of interaction of factors" of a catalyzed chemical reaction (claim 6); (6) analyzing combinatorial results according a relationship $y = X\beta + e$ where X is a matrix of experiment factor and interaction levels, y is a matrix of experimental results, β is effects and e is an error term of variance σ^2 from a normal distribution (claim 18); (7) assembling results as an $n \times 1$ vector y , assembling factor level values into an $n \times k+1$ matrix X , representing extents of the results and factor level values as +1's and -1's

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accordingly and solving for effects parameters β according to the relationship $\beta = (X'X)^{-1}X'y$ where superscript $'$ is a transpose of a matrix and superscript $^{-1}$ identifies an inverse function of a matrix (claims 19 to 21); (8) effecting parallel chemical reactions on a micro scale (claim 23); (9) reacting and identifying tagged reactants and products (claim 25); (10) reiterating a CHTS on an experimental space selected by matrix algebra analysis of first iteration results (claims 26 to 28); and (11) defining an experimental space to "comprise a reactant or catalyst at least partially embodied in a liquid and... contacting the reactant or catalyst with an additional reactant at least partially embodied in a gas, wherein the liquid forms a film having a thickness sufficient to allow a reaction rate that is essentially independent of a mass transfer rate of additional reactant into the liquid to synthesize products that comprise the results" (claim 34).

"A prima facie case of obviousness is established when the teachings from the prior art itself would appear to have suggested the claimed subject matter to a person of ordinary skill in the art...." *In re Rijckaert*, 28 USPQ2d 1955, 1956 (Fed. Cir. 1992). Agrafiotis et al., Grate et al. and Chaudhari et al. fail to teach or suggest any of (1) through (11) above. "If examination... does not produce a prima facie case of unpatentability, then without more the applicant is entitled to grant of the patent." *In re Oetiker*, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992).

The references do not establish a prima facie of obviousness of claims 1 to 7, 9 to 10, 13 to 36 and 39 to 54. For this additional reason, the rejections under 35 U.S.C. 103 should be withdrawn.

IV. IMPROPER FINAL REJECTION

The first Office Action (May 15, 2003) in this case rejected claims 1 to 3, 5 to 11, 13 to 17, 23 to 28, and 34 under 35 U.S.C. 103(a) over Agrafiotis et al. and Grate et al. and claims 1 to 3, 5 to 11, 13 to 17, and 23 to 34 under 35 U.S.C. 103(a) over Agrafiotis et al., Grate et al. and Chaudhari et al. The Office Action did not reject claim 12 under 35 U.S.C. 103(a). Hence to obtain a "quick" allowance, Applicant amended the independent claims to include the claim 12 limitations and the limitations of all intervening claims. Now for the first time, in the Final Rejection the PTO rejects the

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independent claims with the claim 12 and intervening claim limitations under 35 U.S.C. 103(a) over the same art that was previously applied against all the claims except claim 12.

37 C.F.R. § 1.113 entitled "Final rejection or action." provides that "[o]n the second or any subsequent examination or consideration by the examiner the rejection or other action may be made final." The present rejection is the *first* consideration of the limitations of claim 12. Contrary to the PTO's statement,³ the present rejection of the claim 12 limitations was not necessitated by Applicant's amendment of claim 1. The claim 12 limitations have always been in the case. If failure to consider the claim 12 limitations was an oversight by the PTO, then the proper procedure is to reissue the first office action to address the claim 12 limitations and to restart the period for response. A final rejection of any of claim 1, claim 35 or claim 36 – all including the claim 12 limitations - is not authorized under the Rules of practice.

The PTO is respectfully requested to allow the claims or withdraw the present office action and to issue a new non-final office action, restarting the period for response. Toward that end, Applicant requests an interview with the Supervisory Patent Examiner to discuss the 37 C.F.R. § 1.113 propriety of finality of the current office action. Applicant's representative will call the PTO Examiner immediately upon filing this Request for Reconsideration to schedule the interview and in accordance with MPEP 713.04, will provide an "Applicant Initiated Interview Request" form, PTOL-413A prior to the interview.

³ This comment appears in the middle of the office action 35 U.S.C. §112, second paragraph rejection. Applicant believes that this comment is intended to apply to 35 U.S.C. §103(a) rejection. If Applicant is incorrect, then the PTO is respectfully requested to explain the 35 U.S.C. §112, second paragraph relevance.

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V. CONCLUSION

In view of the foregoing amendments and remarks, it is respectfully submitted that claims 1 to 7, 9 to 10 13 to 36 and 39 to 54 are allowable. Reconsideration and allowance are requested.

Should the Examiner believe that any further action is necessary in order to place this application in condition for allowance, he is requested to contact the undersigned at the telephone number listed below.

Respectfully submitted,



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